

**Listing of Claims**

The following listing of claims will replace all prior versions, and listings, of claims in the subject application:

1. (currently amended) A system for determining experimentally a plurality of three-dimensional atomic structures, each of which is associated with a corresponding protein, comprising:

a database of sequence information for a first plurality of proteins, and structural information and functional information for selected a second plurality of proteins;

at least one bioinformatics tool adapted to use the sequence information, structural information and functional information stored in the database to cluster the first plurality of proteins into a plurality of families, in which, for each family, members of the family have homologous sequences;

protein synthesis means for synthesizing for each family determined by the at least one bioinformatics tool a plurality of target proteins which are members of the family, using information stored in the database corresponding to the target proteins, the protein synthesis means having screening means for screening products of the synthesis to choose selected synthesized products, which are effective as the target proteins, for processing;

protein processing means for preparing, purifying and characterizing each of the selected synthesized products screened through the screening means;

crystallization means for crystallizing the processed synthesized product ~~against a plurality of crystallization screens~~ processed by the protein processing means, to produce a plurality of specimen crystals of the target protein, and testing

the plurality of specimen crystals for predetermined diffraction characteristics to determine ~~suitable~~ the specimen crystals which are suitable for diffraction measurement;

X-ray crystallography means for performing high-throughput crystallography on the specimen crystals ~~of each target protein~~ determined by the crystallization means to be suitable for diffraction measurement, the X-ray crystallography means having diffraction measuring means for measuring for diffraction data the suitable specimen crystals of the target protein, analyzing means for analyzing the diffraction data, means for building an atomic model of the target protein according to an analysis of the diffraction data by the analyzing means, and means for refining the model of the target protein against the diffraction data and storing the refined model in the database;

structure extraction means having means for analyzing the refined model of the target protein using sequence information corresponding to other family members which is stored in the database and structural information corresponding to other proteins which is stored in the database, and means for analyzing the refined model for functional motifs and for surface characteristics ~~to define active sites and macromolecular contact sites, and means for defining at least one class of compounds predicted to have binding potency using the active sites information corresponding to the target protein;~~ and

a homology model building tool adapted to use the refined model of the target protein retrieved from the database to develop a homology model of one or more predicted protein structures,

wherein the database is updated using the at least one bioinformatics tool and the developed homology model to link the refined model of the target protein to other databases which store information concerning biological pathways and functional annotation.

2. (previously presented) A system according to claim 1, further comprising:

cryoprotection means for freezing the suitable specimen crystals,

wherein the suitable specimen crystals are frozen by the cryoprotection means before being measured for diffraction data by the diffraction measuring means.

3. (previously presented) A system according to claim 1, wherein

the protein synthesis means includes cloning means for cloning for each family determined by the at least one bioinformatics tool, in parallel, cDNAs corresponding to the appropriately representative family members into a plurality of expression vectors for a plurality of expressions systems,

the screening means screens for expression constructs obtained by the cloning means to determine ones that are effective as proteins, and

the protein processing means processes the expressed proteins determined to be effective by the screening means.

4. (previously presented) A system according to claim 1, wherein

the X-ray crystallography means includes a synchrotron storage ring having undulator beamlines for high-throughput crystallography by a multiwavelength anomalous diffraction method, and

the analyzing means analyzes the diffraction data by a multiwavelength anomalous diffraction phasing method.

5. (previously presented) A system according to claim 4, wherein selenomethionine is incorporated in the synthesized

target proteins by the protein synthesis means, and the analyzing means using the multiwavelength anomalous diffraction phasing method analyzes diffraction data corresponding to selenomethionyl proteins.

6. (previously presented) A system according to claim 1, wherein the homology model developed by the homology model building tool is used in at least one of target selection, drug design, and design of constructs for experimental analysis.

7. (currently amended) A process for determining experimentally a plurality of three-dimensional atomic structures, each of which is associated with a corresponding protein, comprising the steps of:

(a) systematically organizing sequence information for a first plurality of proteins, and structural information and functional information for ~~selected~~ a second plurality of proteins into a database;

(b) clustering the plurality of proteins into a plurality of families, in which, for each family, members of the family have homologous sequences, using at least one bioinformatics tool and the sequence information, structural information and functional information stored in the database;

(c) synthesizing for each family determined in step (b) a plurality of target proteins which are members of the family, using information stored in the database corresponding to the plurality of target proteins, and screening products of the synthesis to choose selected synthesized products, which are effective as the target proteins, for processing;

(d) preparing, purifying and characterizing each synthesized product that is chosen in step (c);

(e) crystallizing the processed synthesized product prepared, purified and characterized in step (d) ~~against a~~

~~plurality of crystallization screens~~ to produce a plurality of specimen crystals of the target protein;

(f) testing the plurality of specimen crystals grown in step (e) for predetermined diffraction characteristics to determine suitable the specimen crystals of the target protein which are suitable for diffraction measurement;

(g) performing high-throughput crystallography, including measuring for diffraction data the specimen crystals determined in step (f) to be suitable for diffraction measurement, building an atomic model of the target protein according to an analysis of the diffraction data, refining the model of the target protein against the diffraction data, and storing the refined model in the database;

(h) analyzing the refined model, stored in the database in step (g), of the target protein using sequence information corresponding to other family members which is stored in the database and structural information corresponding to other proteins which is stored in the database, and analyzing the refined model of the target protein for functional motifs and for surface characteristics ~~to define active sites and macromolecular contact sites, and means for defining at least one class of compounds predicted to have binding potency using the active sites information corresponding to the target protein;~~

(i) developing a homology model of one or more predicted protein structures using computational tools for homology model building and the refined model of the target protein retrieved from the database; and

(j) updating the database by using the at least one bioinformatics tool and the developed homology model; and to link the refined model of the target protein to other databases which store information concerning biological pathways and functional annotation,

~~(j) performing wherein~~ steps (f) through ~~(i)~~ (j) are

repeated for each of the other target proteins.

8. (previously presented) A process according to claim 7, further comprising the step of:

freezing the specimen crystals of the target protein which are determined in step (f) to be suitable,

wherein the suitable specimen crystals are frozen before being measured for the diffraction data in step (g).

9. (previously presented) A process according to claim 7, wherein

step (c) includes cloning for each family determined in step (b), in parallel, cDNAs corresponding to the appropriately representative family members into a plurality of expression vectors for a plurality of expressions systems,

constructs obtained in the cloning are screened for expression to determine the ones that are effective as proteins, and

the expressed proteins determined to be effective are processed in step (d).

10. (previously presented) A process according to claim 7, wherein

the high-throughput crystallography in step (g) is performed using a synchrotron storage ring having undulator beamlines along with a multiwavelength anomalous diffraction method, and

the diffraction data measured in step (g) is analyzed using a multiwavelength anomalous diffraction phasing method.

11. (previously presented) A process according to claim 10, wherein selenomethionine is incorporated in the plurality of target proteins synthesized in step (c), and the multiwavelength anomalous diffraction phasing method is used to analyze

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Serial No.: 09/235,986  
Filed: January 22, 1999  
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diffraction data measured for selenomethionyl proteins.

12. (previously presented) A process according to claim 7, further comprising the step of

using the homology model developed in step (i) in at least one of target selection, drug design, and design of constructs for experimental analysis.